REMARKS

Applicants respectfully note that Applicants' Amendment filed August 1, 2001, was *not* entered by the PTO. Following entry of Applicants' Supplemental Amendment dated November 17, 2000, Claims 1-11, 13-15, 21-36, 40, 41, 44, 50-52, 58-60 and 62-67 were pending and under consideration in the instant application. With the instant Amendment, Claims 1, 50, 52 and 58-60 are amended. For the PTO's convenience, a clean copy of pending Claims 1-11, 13-15, 21-36, 40, 41, 44, 50-52 and 58-60, 62-67 is attached hereto as Exhibit B.

Applicants respectfully note that Claim 44 is pending and under consideration in the instant application. Although the PTO examined Claim 44 in the final Office Action mailed February 1, 2001, Claim 44 is not indicated on the Office Action Summary.

Applicants expressly reserve the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

I. THE AMENDMENT OF THE CLAIMS

Claims 1, 50, 52 and 58-60 have been amended to recite with greater particularity certain features of Applicants' invention.

The amendments are fully supported by the specification and claims as originally filed. For example, support for the amendments to Claims 1 and 60 can be found in the specification at page 11, line 29, through page 12, line 14. The amendment of Claim 58 is supported, for example, at page 14, lines 2-3, and at page 28, lines 4-5. The amendment of Claim 59 is supported, for example, at page 17, line 2. Claims 50 and 52 have been amended merely to depend from pending Claims 1, 58, 59 or 60.

As the amendments to the claims are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry thereof is therefore respectfully requested.

II. CLAIM OBJECTIONS

Claims 4 and 28 stand objected to as allegedly being of improper dependent form. The PTO asserts that Claims 4 and 28 improperly depend from Claim 1. Applicants

respectfully note that pending Claims 4 and 28 do not depend from Claim 1. Applicants therefore respectfully request that the objections to Claims 4 and 28 be withdrawn.

III. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

A. The Rejections of Claims 2-10, 13-15, 21, 22, 24-36, 40, 41, 44, 59 and 63

Claims 2-10, 13-15, 21, 22, 24-36, 40, 41, 44, 59 and 63 stand rejected under 35 U.S.C. § 112 as allegedly being indefinite. The PTO asserts that Claim 59 is indefinite over the phrase "substantially irreversibly." Claims 2-10, 13-15, 21, 22, 24-36, 40, 41, 44 and 63 depend from Claim 59. Applicants submit that amended Claim 59 does not recite the phrase "substantially irreversibly" and meets the requirements for patentability under 35 U.S.C. § 112. Applicants respectfully request that the rejections of Claims 2-10, 13-15, 21, 22, 24-36, 40, 41, 44, 59 and 63 under 35 U.S.C. § 112 be withdrawn. Applicants respectfully note that no further rejections of Claim 59 are outstanding.

B. The Rejections of Claims 10, 34 and 67

Claims 10, 34 and 67 stand rejected under 35 U.S.C. § 112 as allegedly being indefinite. The PTO asserts that the term "high density or high molecular weight" renders the claims indefinite.

35 U.S.C. § 112, second paragraph, states that the specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. According to the Federal Circuit, the "distinctly claiming" requirement means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. *See Miles Laboratories, Inc. v. Shandon Inc.*, 27 USPQ2d 1123, 1125-26 (Fed. Cir. 1993). The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *See id.* If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, 35 U.S.C. § 112 demands no more. *See id.*

Applicants submit that Claims 10, 34 and 67 reasonably apprise those skilled in the art of their scope. Claims 10, 34 and 67 recite a flow-through device comprising a porous substrate composed of high density polyethylene ("HDPE") or ultra-high molecular weight

polyethylene ("UHMWPE"). The terms high density polyethylene and ultra-high molecular weight polyethylene are well known to those of skill in the art as evidenced by Exhibit B of the Amendment Under 37 CFR § 1.112 filed by the Applicants on December 3, 1998. Because the terms are so well known, one of skill in the art would be immediately apprised of their scope upon reading Claims 10, 34 and 67.

Applicants thus submit that Claims 10, 34 and 67 are definite and respectfully request that the rejection of these claims under 35 U.S.C. § 112 be withdrawn.

C. The Rejections of Claims 24, 25 and 36

Claims 24, 25 and 36 stand rejected under 35 U.S.C. § 112 as allegedly being indefinite. The PTO asserts that the term "high stringency or low stringency or moderate stringency" renders the claims indefinite.

Applicants submit that Claims 24, 25 and 36 reasonably apprise those of skill in the art. First, the terms "high stringency," "low stringency" and "moderate stringency" are well known to those of skill in the art as evidenced by Exhibit C of the Amendment Under 37 CFR § 1.112 filed by the Applicants on December 3, 1998. Because the terms are so well known, one of skill in the art would be immediately apprised of their scope upon reading Claims 24, 25 and 36.

Second, when read in light of the specification, Claims 24, 25 and 36 are definite. The specification provides extensive descriptions of the terms "high stringency," "low stringency" and "moderate stringency." The term "high stringency" is defined and discussed in detail in the specification at page 32, line 33, through page 33, line 9. The terms "moderate stringency" and "low stringency" are defined and discussed in detail in the specification at page 33, lines 10-25. Examples of useful hybridization conditions are provided in the specification at page 33, line 26, through page 34, line 20. In particular, specific examples of high stringency conditions, moderate stringency conditions and low stringency conditions are provided at page 34, lines 9-13. The specification thus provides detailed definitions, discussions and even specific examples that apprise one of skill in the art of the meaning of the terms "high stringency," "low stringency" and "moderate stringency." Thus, one of skill in the art would be apprised of the scope of the terms upon reading Claims 24, 25 and 36 in light of the specification.

Applicants submit that one of skill in the art, upon reading Claims 24, 25 and 36 in light of the specification, would be readily apprised of the scope of Claims 24, 25 and 36. Applicants respectfully request that the rejection of Claims 24, 25 and 36 under 35 U.S.C. § 112 be withdrawn.

IV. THE REJECTIONS UNDER 35 U.S.C. § 102

A. Beattie Does Not Teach Each and Every Element of Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64

Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 5,843,767 ("Beattie"). Applicants traverse the rejections of Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64 on the ground that Beattie does not teach or suggest each and every element of Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64.

The standard for anticipation under 35 U.S.C. §102 is strict identity. Anticipation under § 102 can only be established by a single prior art reference that teaches each and every element of the claimed invention. *Structural Rubber Products Co. v. Park Rubber Co.* 223 USPQ 1264 (1984).

Beattie does not teach the flow through devices recited in the claims as pending after entry of the Supplemental Amendment filed by Applicants November 17, 2001. For instance, Beattie does not teach porous substrates comprising capture polynucleotides having the pore sizes, porosities and/or capture polynucleotide densities recited in the claims as pending after entry of the Supplemental Amendment filed by Applicants November 17, 2001. Nevertheless, in order to expedite prosecution, Applicants have amended Claims 1 and 60 to secure rapid allowance of the claims.

Beattie does not teach each and every element of Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64. Amended Claims 1, 58 and 60 recite flow-through devices comprising a porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene. The polymeric materials of Claims 1, 58 and 60 can provide materials that do not deform and that remain solid while in use. Claim 59 recites a flow-through device activated by plasma activation. Plasma activation is capable of reproducibly generating a uniformly high density of reactive groups on the surface of a porous substrate for a flow through device of the present invention.

Claims 2-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41 and 64 depend from one or more of Claims 1, 58, 59 and 60.

Beattie does not teach a flow-through device comprising a porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene, nor does Beattie teach a flow-through device activated by plasma activation. Beattie teaches instead nanochannel glass wafers that are activated by conventional chemical methods. Beattie does not consider the materials recited in Claims 1, 58 and 60.

Furthermore, Beattie does not teach activation by a method as robust as plasma activation. In fact, the only method that Beattie even contemplates for attaching oligonucleotides to the silicon wafers is via epoxysilane activation. Beattie clearly does not teach or suggest plasma activation of a porous substrate.

Beattie, therefore, does not teach each and every element of Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60 and 64. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102.

B. Kamb Does Not Teach Each and Every Element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62

Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,060,240 ("Kamb"). Applicants traverse the rejection of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 on the ground that Kamb does not teach or suggest each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62.

As noted above, the standard for anticipation under 35 U.S.C. §102 is strict identity. Anticipation under § 102 can only be established by a single prior art reference that teaches each and every element of the claimed invention. *Structural Rubber Products Co. v. Park Rubber Co.* 223 USPQ 1264 (1984).

Kamb does not teach porous substrates comprising capture polynucleotides having the pore sizes, porosities and/or capture polynucleotide densities recited in the claims as pending after entry of the Supplemental Amendment filed by Applicants November 17, 2001. Nevertheless, in order to expedite prosecution, Applicants have amended Claim 58 to

expedite prosecution and secure rapid allowance of the claims. Amended Claim 58 recites flow-through device comprising a three-dimensional porous macroscopic network in order to emphasize the unitary nature of the device.

Kamb does not teach each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62. Amended Claim 58 recites a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide. Independent Claims 1, 59 and 60 do not stand rejected over Kamb. Claims 3-11, 14, 15, 22-25, 28-36, 40, 41 and 62 depend from one or more of Claims 1, 58, 59 and 60.

Kamb does not teach or suggest a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide. What Kamb teaches is an individual bead that might have an oligonucleotide attached and collections of such beads. However, Kamb nowhere teaches any porous macroscopic network that has a capture polynucleotide immobilized thereon. Kamb simply does not consider porous macroscopic networks for immobilization of polynucleotides. As such, Kamb cannot teach or suggest each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41 and 62.

Since Kamb does not teach or suggest each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41 and 62, Kamb does not anticipate Claims 3-11, 14, 15, 22-25, 28-36, 40, 41 and 62. Applicants request that the rejection of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41 and 62 under 35 U.S.C. § 102 be withdrawn.

V. THE REJECTIONS UNDER 35 U.S.C. § 103

Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,060,240 ("Kamb"). Claims 44, 50-52 and 65 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Beattie and U.S. Patent No. 5,843,662 ("Dean"). Claims 50-52 and 65-67 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kamb and U.S. Patent No. 5,843,662 ("Dean"). The rejections are respectfully traversed on the ground that Beattie, Kamb and Dean are not

sufficient to establish a *prima facie* case of obviousness against Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 44, 50-52, 58, 62 and 65-67.

A. The Legal Standard of *Prima Facie* Obviousness

To reject claims in an application under 35 U.S.C. § 103, the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); MPEP § 2142. In the absence of establishing a proper *prima facie* case of obviousness, applicants who comply with the other statutory requirements are entitled to a patent. *In re Oetiker*, 24 USPQ2d. 1443, 1444 (Fed. Cir. 1992).

In order to establish *prima facie* obviousness, three basic criteria must be met. First, the prior art must provide one of ordinary skill in the art with a suggestion or motivation to modify or combine the teachings of the references relied upon by the PTO to arrive at the claimed invention. When an obviousness determination relies on one reference, there must be suggestion or motivation to modify the teaching of the reference in the manner suggested by the PTO. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985). Alternatively, when an obviousness determination relies on a combination of two or more references, there must be some suggestion or motivation to combine the references. *WMS Gaming Inc. v. International Game Technology*, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999). The suggestion or motivation to combine the references generally arises in the references themselves, but may also be inferred from the nature of the problem or occasionally from the knowledge of those of ordinary skill in the art. *See id.* The mere fact that references *could* be modified or combined does not render the resultant modification or combination obvious unless the prior art also suggests the desirability of the modification or combination. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP § 2143.01.

Second, the prior art must provide one of ordinary skill in the art with a reasonable expectation of success. Thus, the skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested by the PTO would succeed. *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988).

Third, the prior art, either alone or in combination, must teach or suggest each and every limitation of the rejected claims. *In re Gartside* , 53 USPQ2d 1769 (Fed. Cir. 2000). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, not Applicants' disclosure. *In re Vaeck*,

20 USPQ2d 1438 (Fed. Cir. 1991). If *any one* of these criteria are not met, *prima facie* obviousness is not established, and Applicants are *not* required to show new or unanticipated results. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985).

B. Kamb Is Not Sufficient to Render Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 *Prima Facie* Obvious

As discussed in section A, above, in order to render Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 *prima facie* obvious, Kamb must teach or suggest each and every element of those claims. As discussed in Section IV, above, each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 are not taught or suggested by Kamb. For example, Kamb does not teach or suggest a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide.

Since Kamb fails to teach or suggest a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide, Kamb fails to teach or suggest each and every element of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 and is not sufficient to render the claims *prima facie* obvious. Applicants respectfully request that the rejection of Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58 and 62 under 35 U.S.C. § 103 be withdrawn.

C. Beattie and Dean Are Not Sufficient to Render Claims 44, 50-52 and 65 *Prima Facie* Obvious

As discussed in section A, above, in order to render Claims 44, 50-52 and 65 *prima facie* obvious, Beattie must teach or suggest each and every element of those claims. For the reasons discussed in Section IV, above, each and every element of Claims 44, 50-52 and 65 are not taught or suggested by Beattie. In particular, Claims 44, 50-52 and 65 depend from Claims 1, 58, 59 and 60. For the reasons discussed above Beattie does not teach or suggest each and every element of Claims 1, 58, 59 and 60. For example, Beattie does not teach or suggest a flow-through device comprising a porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene, nor does Beattie teach a flow-through device activated by plasma activation.

These deficiencies in Beattie are not cured by Dean because Dean also does not teach or suggest a flow-through device comprising a porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene, or a flow-through device activated by plasma activation. Dean teaches a kit for determining nucleic acid concentration in a nucleic acid solution. The kit comprises a nucleic acid support such as a nylon membrane for retaining a nucleic acid. According to the methods taught by Dean, nucleic acids are applied directly to the support with no activation of the support whatsoever. Dean thus does not teach or suggest a flow-through device comprising a porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene, or a flow-through device activated by plasma activation.

Since Beattie and Dean, alone or in any combination, fail to teach or suggest plasma activation of a porous substrate, Beattie and Dean fail to teach or suggest each and every element of Claims 44, 50-52 and 65 and are not sufficient to render the claims *prima facie* obvious. Applicants respectfully request that the rejection of Claims 44, 50-52 and 65 under 35 U.S.C. § 103 be withdrawn.

D. Kamb and Dean Are Not Sufficient to Render Claims 50-52 and 65-67 *Prima Facie* Obvious

As discussed in section A, above, in order to render Claims 50-52 and 65-67 *prima facie* obvious, Kamb and Dean must teach or suggest each and every element of those claims. Claims 50-52 and 65-67 depend from Claims 1, 58, 59 and 60, and Kamb does not teach or suggest each and every element of Claims 1, 58, 59 or 60 for the reasons discussed above. For example, Kamb does not teach or suggest a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide. In addition, for the reasons discussed in Section C, above, each and every element of Claims 50-52 and 65-67 are not taught or suggested by Dean. For example, Dean also does not teach or suggest a flow-through device comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide.

Since Kamb and Dean, alone or in any combination, fail to teach or suggest plasma activation of a porous substrate, Kamb and Dean fail to teach or suggest each and every element of Claims 50-52 and 65-67 and are not sufficient to render the claims *prima facie*

obvious. Applicants respectfully request that the rejection of Claims 50-52 and 65-67 under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

Applicants submit that Claims 1-11, 13-15, 21-36, 40, 41, 44, 50-52, 58-60 and 62-67 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1-11, 13-15, 21-36, 40, 41, 44, 50-52, 58-60 and 62-67 to issuance is therefore kindly solicited.

No fees in addition to the appeal and extension fees are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds U.S. Deposit Account No. 16-1150.

Respectfully submitted,

Date: March 1, 2002

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Enclosure (Exhibits A and B)

EXHIBIT A
MARKED UP VERSION OF AMENDED CLAIMS

1. (Three times amended) A flow-through device for capturing a target nucleic acid comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, and wherein said porous substrate is about 1 mm to 20 mm thick.

50. (Three Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) [a three-dimensional porous substrate having an average pore size of about 10 μm to about 100 μm and a porosity in the range of 25% to 80%] a flow-through device according to Claims 1, 58, 59 or 60; and

b) a capture polynucleotide capable of being covalently attached to the porous substrate.

52. (Three Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) [a three-dimensional porous substrate having an average pore size of about 10 μm to about 100 μm and a porosity in the range of 25% to 80%] a flow-through device according to Claims 1, 58, 59 or 60; and

b) means for generating a capture polynucleotide which is capable of hybridizing to the target nucleic acid and which is capable of being covalently attached to the porous substrate.

58. (Twice Amended) A flow-through device for capturing a target nucleic acid comprising a three-dimensional porous [substrate] macroscopic network having immobilized thereon a capture polynucleotide which is capable of hybridizing to the target nucleic acid, and wherein said porous substrate is composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene.

59. (Twice Amended) A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate having [substantially irreversibly] covalently immobilized thereon a capture polynucleotide which is capable of hybridizing to the target nucleic acid, wherein said porous substrate, prior to immobilization of the capture polynucleotide, is activated by plasma activation.

60. (Twice amended) A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and a porosity in the range of about 25 to 80% and having immobilized thereon a capture polynucleotide capable of hybridizing to the target nucleic acid.

EXHIBIT B
PENDING CLAIMS AFTER ENTRY OF INSTANT AMENDMENT

1. (Three times amended) A flow-through device for capturing a target nucleic acid comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, and wherein said porous substrate is about 1 mm to 20 mm thick.

2. (Twice Amended) The flow-through device of Claim 58, 59 or 60 in which said porous substrate is about 1 mm to 20 mm thick.

3. (Twice Amended) The flow-through device of Claim 1, 58 or 59 in which said porous substrate has an average pore size of about 1 μm to about 250 μm.

4. (Twice Amended) The flow-through device of Claim 58, 59 or 60 in which said porous substrate has immobilized thereon about 2×10^{-19} to 2×10^{-15} nmol/nm^2 of said capture polynucleotide.

5. (Amended) The flow-through device of Claim 1, 58, 59 or 60 in which said capture polynucleotide is covalently attached to the porous substrate.

6. (Amended) The flow-through device of Claim 1, 58, 59 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a phosphodiester, phosphorothioate or phosphoramidate linkage.

7. (Amended) The flow-through device of Claim 1, 58, 59 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a carboxyamide linkage.

8. (Twice Amended) The flow-through device of Claim 1, 58, 59 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a linker.

9. (Twice Amended) The flow-through device of Claim 1, 59 or 60 in which said porous substrate is composed of glass or a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene.

10. (Thrice Amended) The flow-through device of Claim 1, 58, 59 or 60 in which said porous substrate is composed of high density or ultra-high molecular weight polyethylene.

11. (Twice Amended) The flow-through device of Claim 1, 58 or 60 in which said porous substrate has a void volume in the range of about 1 $\mu l/cm^2$ to about 100 $\mu l/cm^2$.

13. (Twice Amended) The flow-through device of Claim 1, 58 or 59 in which the porous substrate has a porosity in the range of about 25 to 80%.

14. (Twice Amended) The flow-through device of Claim 1, 58, 59 or 60 in which the capture polynucleotide is covalently immobilized on the porous substrate via its 5'- or 3'-terminal residue.

15. The flow-through device of Claim 14 further including a linker disposed between the porous substrate and the capture polynucleotide.

21. (Twice Amended) The flow-through device according to Claim 1, 58, 59 or 60 further comprising a housing in which the three-dimensional porous substrate is disposed.

22. (Amended) The flow-through device of Claim 21, in which said housing is selected from the group consisting of a syringe barrel, a pipette, a disposable pipette tip, a chromatography column, a spin column, a microchannel, a capillary and a multi-well plate.

23. (Amended) A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 1 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

24. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said target nucleic acid is applied to said flow-through device under conditions of high stringency.

25. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said target nucleic acid is applied to said flow-through device under conditions of low stringency.

26. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said target nucleic acid is applied to the flow-through device under conditions wherein it hybridizes with said capture polynucleotide in less than one minute.

27. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said porous substrate of said flow-through device has an average pore size of about 1 μm to about 250 μm.

28. (Twice Amended) The method of Claim 62, 63 or 64 in which the density or surface concentration of said capture polynucleotide is about 2×10^{-19} to 2×10^{-15} nmol/nm^2.

29. (Amended) The method of Claim 23, 62, 63 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device.

30. (Amended) The method of Claim 23, 62, 63 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a phosphodiester, phosphorothioate or phosphoramidate linkage.

31. (Amended) The method of Claim 23, 62, 63 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a carboxyamide linkage.

32. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a linker.

33. (Twice Amended) The method of Claim 23, 63 or 64 in which said porous substrate of said flow-through device is composed of glass or a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene.

34. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said porous substrate of said flow-through device is composed of high density or ultra-high molecular weight polyethylene.

35. (Twice Amended) The method of Claim 23, 62, 63 or 64 in which said porous substrate of said flow-through device has a void volume in the range of 0.1 $\mu l/cm^2$ to about 100 $\mu l/cm^2$.

36. (Twice Amended) The method of Claim 23, 62, 63 or 64 which further includes the step of washing said hybridized complex under conditions of moderate or high stringency.

40. (Twice Amended) A method of determining whether a sample contains a target nucleic acid, said method comprising the steps of:

(a) flowing a sample suspected of containing a target nucleic acid through a flow-through device according to Claim 1, 58, 59 or 60 under conditions wherein the target nucleic acid and capture polynucleotide hybridize; and

(b) detecting the presence of hybrids, wherein a positive detection indicates the presence of the target nucleic acid in the sample.

41. The method of Claim 40, in which said target nucleic acid bears a reporter moiety and hybrids are detected by detecting the presence of said reporter moiety.

44. (Twice Amended) A kit for capturing a target nucleic acid of interest from a sample, comprising:

a) a flow-through device according to Claim 1, 58, 59 or 60; and

b) a housing into which the flow-through device can be disposed.

50. (Three Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) a flow-through device according to Claims 1, 58, 59 or 60; and

b) a capture polynucleotide capable of being covalently attached to the porous substrate.

51. The kit of Claim 50 further including a linker capable of being covalently attached to the porous substrate and the capture polynucleotide.

52. (Three Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) a flow-through device according to Claims 1, 58, 59 or 60; and

b) means for generating a capture polynucleotide which is capable of hybridizing to the target nucleic acid and which is capable of being covalently attached to the porous substrate.

58. (Twice Amended) A flow-through device for capturing a target nucleic acid comprising a three-dimensional porous macroscopic network having immobilized thereon a capture polynucleotide which is capable of hybridizing to the target nucleic acid, and wherein said porous substrate is composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene.

59. (Twice Amended) A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate having covalently immobilized thereon a capture polynucleotide which is capable of hybridizing to the target nucleic acid, wherein said porous substrate, prior to immobilization of the capture polynucleotide, is activated by plasma activation.

60. (Twice amended) A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and a porosity in the range of about 25 to 80% and having immobilized thereon a capture polynucleotide capable of hybridizing to the target nucleic acid.

62. A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 58 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

63. A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 59 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

64. A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 60 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

65. The kit of Claim 50 or 51 in which the porous substrate is activated with about 6×10^{-17} to 9×10^{-15} nmol/nm^2 of a reactive group.

66. The kit of Claim 50 or 51 in which the porous substrate is composed of glass or a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene.

67. (Amended) The kit of Claim 66 in which the porous substrate is composed of high density or ultra-high molecular weight polyethylene.